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(56) Documents Cited
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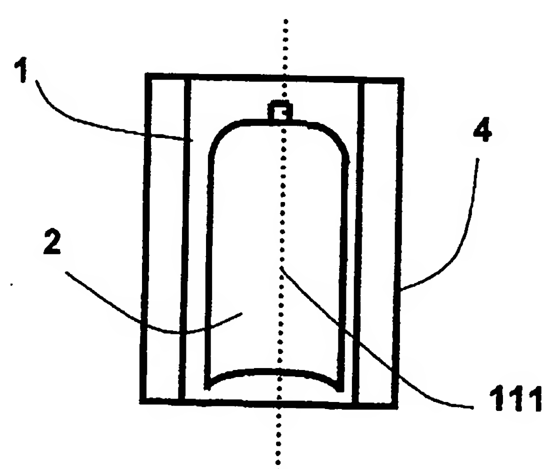
(54) Abstract Title
Leak testing a pharmaceutical product

(57) Device for automated collection and detection of gaseous material leaking from individual MDI (metered dose inhaler) cans that have been filled and sealed on high-speed production lines. Individual test chambers carry a unique ID Tag and detection system includes self-diagnostic and test aids. An isolation chamber 1 may totally enclose the item 2 being tested, or partially enclose it (figure 4). Gas detection means and gas circulation means may be incorporated into the isolation chamber means.

Figure 3



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The claims were filed later than the filing date but within the period prescribed by Rule 25(1) of the Patents Rules 1995.

Figure 1

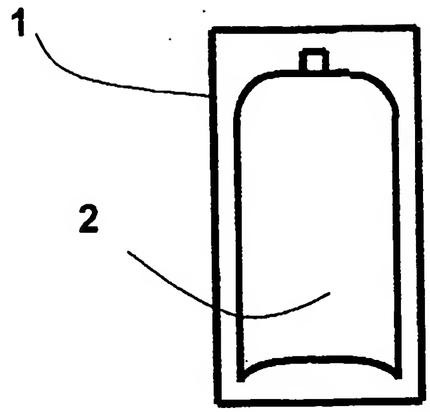


Figure 2

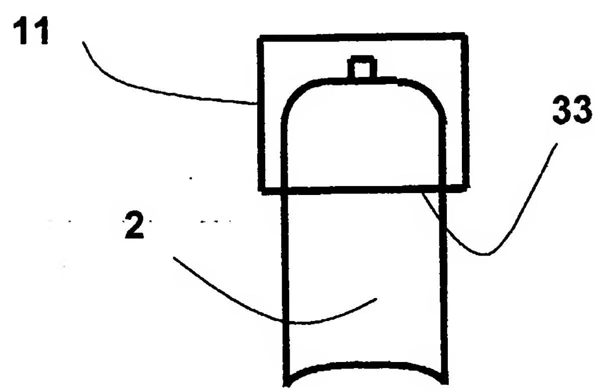


Figure 3

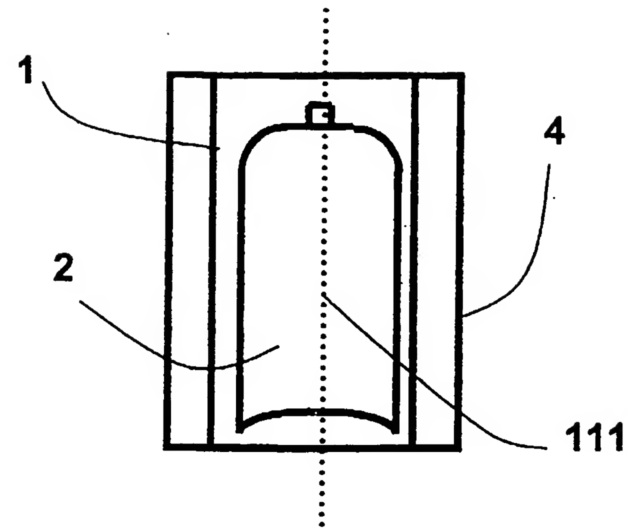
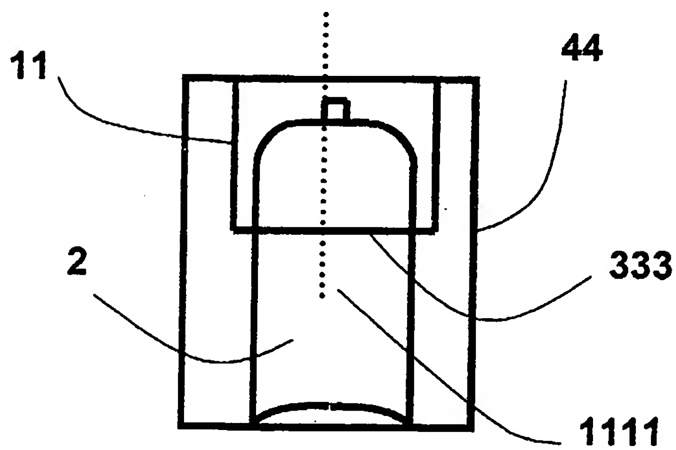


Figure 4



Detection of MDI leaks

Background

In several production industries, e.g. pharmaceutical metered dose inhaler (MDI) filled with refrigerant propellants, there is a need to establish integrity of aerosol cans before packing, because of the risks that MDI products would fail to work properly. High production and 100% validation need automatic testing.

Free air refrigerant gas sniffing sensors generally perform at the 0.1% level of air concentration, which is used for overall safety detection in factory facilities but not for on-line testing and 100% validation of the products themselves. Some other very specific gas sensing types may be rather sensitive but also expensive, work for troubleshooting and leak location not for whole products.

So the most common methods of detecting significant leaks in a particular can are by inspection of the packages and weighing them knowing the fill weight: a very common criterion is by the measured weight loss over 7-day storage. The following section discusses the extent necessary for real improvements.

Current online weighing methods may achieve filled MDI weight determination to typically ±0.1 g or so, whereas the typical leak specification is < 0.7 g per year weight loss, being 5% of the tare weight. Reweighing needs many lines, as the significant time required for weight losses to become detectable with this method is totally inconsistent with the filling rate in MDI production lines.

On-line leak test machines actually operate with a leak measurement period of a few seconds, not a few minutes, when faced with production line speeds of several products per second. Pharmaceutical lines can run 10 times faster.

The present invention concerns the design of a combined accumulation test chamber for detection of leakage of propellant materials from MDI or similar. These chambers can be used in leak test systems, designed for the validation of filled aerosol can integrity, that are described here, by me, and elsewhere. They might also be used in existing, suitably modified, leak detection systems.

The accumulation volume and the time elapsed are central to this method of leak detection using a gas sensor with a minimum detection threshold, usually measured in ppm, parts per million by volume in air, for the leakage material.

The maximum allowed material leak rate (g/year) and the minimum detector sensitivity (ppm) needed for gas of molecular weight M can be deduced from the concentration rise (%v/v) in accumulation volume (mL) and conversions appropriate to room temperature and the fundamental gas laws of physics:

Mass leakage (g/y) x Time (min) = Volume (mL) x concentration shift (%v/v)

x M / 4.6

For optimum CFC-replacement propellant with M=170, the required minimum gas detector sensitivity is about 10 ppm for an accumulation volume of 2.7 mL with accumulation periods of 1 minute to provide a basic resolution of 0.1g/y.

As has been stated previously, the time available for conventional testing is usually a few seconds and not minutes. During such a time the component under validation must be assessed for total leakage at a level of < 300 ppb. Conventional gas sensing technology used conventionally cannot detect the chosen material at the level of 30 ppm let alone 100 times better at 300 ppb.

Even commercial quadrupole and time of flight mass spectrometer systems are struggling to make a better measurement than this at the production rates of MDI lines. This is generally because the systems are quite large and they require a gas inlet into their high vacuum detection system, and this inlet is inefficient and slow. They normally require about 10 seconds or so of signal.

These gas inlet systems themselves have an internal volume that has to be displaced before the required signal reaches the sensing region for detection and introduce severe problems for this time and sensitivity limited application. Generally they would therefore be avoided or designed out where possible.

Should the signal be required faster, increasing the gas flow rate through the inlet would help in free air, but if this rate has to be supplied from the sealed accumulation chamber it will be depleted faster, whereas if this accumulation chamber is deliberately or actually leaking air from elsewhere it will be diluted.

Likewise, conventional sensor response times are much slower than a second and this technology must now be used in rather novel ways. In proposed leak test systems using the integrated sensor and accumulation volume to hold the component under test for periods of typically a minute or more, the technical problems are effectively reduced to maintaining the sensor stability over time.

Gas detector stability has very often plagued the refrigerant leak detection application, and most especially with hand-held battery powered equipment which is designed to be switched on and used sensitively at very short notice. Response in particular could be found to vary depending with switch on time, storage conditions when off and previous exposure to gross refrigerant leaks.

Some of the findings of this work are applicable to one particular example of this present invention, and may prove beneficial to implementation, although they were not aimed at the MDI validation invention or the present invention. Their particular advantages are their availability and relatively low cost for the implementation, and ease of adaptation for use, within the present invention.

This becomes important when considering perhaps hundreds are required per validation machine in order to cope with the MDI production line requirements, for example 600 needed for a 0.1 g/yr resolution at 30ppm gas detection level. Commercial considerations would probably limit the chambers to the smallest numbers providing a "6-sigma" confidence level for the MDI validation system.

Essential features

The present invention requires a chamber which partially or totally encloses the component under test, preferably with a minimum volume consistent with handling the component at high speed without damage and allowing all the leaking gaseous or vapour material around the component to fill this volume.

Assembly is designed for accumulation testing within MDI leak test machine designs, described elsewhere, for the validation of filled aerosol can integrity, but could also be incorporated into existing, suitably modified, test machines with additional of accumulator sections such as a spiral or a cartridge system.

An integral gas sensor is incorporated such that it detects, with suitable flow means circulating and mixing any leaking material to a more uniform mixture with the previous background air or gas, leaks into the accumulation volume. This sensing and flow combination does not actually extract any material from the accumulation volume, but keeps returning it into the accumulation volume.

The chamber system carries a unique "ID" tag, that can be read or indicated or transmitted to the control system of a leak test system means provided elsewhere, in order to help provide a tracking means for the MDI contained within the accumulation chamber for timing or sequencing purposes.

The design has integrated gas sensor and electronic drive circuit means, the gas flow means and power supply means, with scope for other attachments, which might be total or partial chambers, palletising clamps or other means.

Partial chambers provide sealing sufficiently robust so as not to damage the MDI product packaging but accommodate the dimensional design tolerances.

Important features

There is a battery powered gas sensing system, which can also transmit or indicate or do both for information on its operational status and that of the sensor signal compared with an inbuilt (several ppm) detection threshold.

The battery power supply may be inductively or otherwise recharged, once detected at a low condition, by an independent means provided elsewhere.

The "ID" tag is available to be read or interrogated at any time, by a means connected to the control system of a leak test system provided elsewhere, for tracking problems associated with the sensor or of the chamber itself or both.

Total chambers may have "in-fills" to minimise the accumulation volume so that the same chambers may be used with MDI products of various heights and diameters and there may be adjustable diameter seals for this purpose.

Introduction to the drawings

The following brief introductions are referenced to the numbering system shown in the drawings, which depict arrangements for ease of understanding. More common features, such as marking and power supplies, are not shown.

Figure 1 shows one typical configuration of prior art using pressure sensors. The accumulation chamber means (1) totally encloses the item under test (2). The orientation of the combined chamber and part as shown is not specific, although it may be considered favourable for both loading and unloading. The profile of the chamber means (1) may need to ensure that the item under test (2) cannot self actuate thereby releasing material into the chamber means (1) during all subsequent periods of testing or handling.

Figure 2 shows another configuration of the prior art using pressure sensors. The accumulation chamber means (11) partially encloses the item under test (2) by having a sufficient seal means (33) around part of the circumference of the item under test (2). The orientation of the combined chamber and part as shown is not specific, although it may be considered favourable for loading. The profile of the chamber means (11) may need to ensure that the item under test (2) cannot self actuate thereby releasing material into the chamber means (11) during all subsequent periods of testing or handling.

Figure 3 shows an integrated combination concept of the present invention. The isolation chamber means (1) totally encloses the item under test (2). Additional gas detection means (4) is in close communication with the contents of the isolation chamber means (1) and may form part of the latter. Gas circulation means (4) may also be incorporated within the housing (4), since in the present invention all gas is returned into the chamber means (1). The orientation of combined detection and circulation, chamber and part as shown is not specific, although it may be considered favourable for handling and for loading and unloading if the housing (4) is evenly distributed around the chamber axis (111) as an annulus as shown, or as one or more end disks.

Figure 4 shows an integrated combination concept of the present invention. The isolation chamber means (11) partially encloses the item under test (2) by having a sufficient seal means (333) around part of the circumference of the item under test (2). Gas detection and gas circulation means (44) is in close communication with the contents of the isolation chamber means (11) and may form part of the latter. The orientation of the combined detection and circulation, chamber and part as shown is not specific, although it may be considered favourable for loading. The orientation of combined detection means, chamber and part as shown is not specific, although preferably the housing of means (44) should be evenly distributed around chamber axis (1111) and extended beyond the seal (333) as far as the base of item under test (2) as shown, or even beyond this level.

Particular examples

The present invention may be performed in the following manner by way of example, referring to the important features as indicated in the drawings.

A combined chamber and detection system and gas circulation means of Figure 4 is applied to the detection of propellant gas leakage from MDIs.

It is convenient to utilise a Bosch type pallet handling system with tagging. This enables the isolation chamber (11) to hold the MDI vertically as shown but with the seal means (333) on the shoulder of the MDI item under test (2) and the housing (4) anchoring the whole assembly to the pallet base.

The tagging system is monitored for the start and finish times for the leakage accumulation measurement as described earlier, although intermediate alarms can be detected both for gross leak and for detection system failures.

Multiples of this system can be incorporated into production line systems such as those by Wilco AG now familiar in on-line liquid filled pouch leak testing. These systems have the capability of taking a combined detection system following the present invention "off line" for reconditioning or recharging and then re-inserting the combined detection system back into the production line.

A particular design suitable for common MDI types filled with R134a type propellants incorporates a common Figaro refrigerant gas sensor type such as used in the ION Science Ltd R2p series handheld leak detector devices.

Within the present design the detection capability of the refrigerant gas sensor is particularly well maintained by continuously powering the sensor means, which is not normally feasible with battery-powered portables such as R2p.

By having an integrated rechargeable battery supply and on-board battery status monitoring, the tagged combination of detection system and chamber is readily checked for the condition of the gas sensing circuitry including power.

The gas sample is drawn across the detector means by a close-coupled fan or pump means having gas exiting from this detection volume conducted back into the isolation chamber (11), thereby maintaining a closed system with the active circulation of an increasingly high concentration of any leakage gas past the detection sensor throughout the period of isolation. The module housing (4) is arranged around the isolation chamber axis (1111) for stability.

In order to reduce the costs of change for MDI of different dimensions, the housing (4) and chambers (11) are constructed to use common parts for the gas detection and circulation means and power supplies, even when there is a need to accommodate MDIs (2) of various diameters. Using such methods is now common, as for example in the machines of Pamasol AG incorporating ION Science Ltd Photec technology for hydrocarbon filled aerosol can leak detection, but may have a practical utility when multiple chambers are used.

CLAIMS

1 A device that totally encloses the individual can under test and includes an integral gas circulation and detection means for the gaseous materials escaping from the can during a timed period.

2 A device that partially encloses the can under test to achieve the same objective as claim 1 but over a restricted portion of the can.

3 A device that has been specifically shaped for the dimensions of a product to provide a minimum volume isolation chamber consistent with collection and detection of leaking gas as in claim 1 or claim 2

4 A device where the product tested is a metered dose inhaler and following claim 1 or 2.

5 A device where the product tested is a metered dose inhaler and following claim 3

6 A device where the gas circulation means is separate from the isolation chamber means of claim 1

7 A device where the gas circulation means is separate from the isolation chamber means of claim 2

8 A device where the detection means is separate from the isolation chamber means of claim 1

9 A device where the detection means is separate from the isolation chamber means of claim 2

10 A device where the gas circulation and detection means are separate from the isolation chamber means of claim 1

11 A device where the gas circulation and detection means are separate from the isolation chamber means of claim 2

12 A device in which the detection means of claim 1 are arranged as annular or disk sections about the axis of the isolation chamber

13 A device in which the detection means of claim 2 are arranged as annular or disk sections about the axis of the isolation chamber

14 A device in which in any of the above claims there are self-test and diagnostic aids, including individual test chamber timing and ID tag.

15 A device in which in any of the above claims there is rechargeable power supply means to continually power the gas detection means.

The Patent Office

INVESTOR IN PEOPLE

Application No:	GB 0115154.7	**Examiner:**	Michael Walker
Claims searched:	ALL	**Date of search:**	20 May 2002

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.T): G1S (SRE, SRL, SRR, SRS, SRX)

Int Cl (Ed.7): G01M 3/16, 3/26, 3/32

Other: On-line: EPODOC, WPI, JAPIO

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X,Y	GB 2345969 A	(ION SCIENCE LTD) whole document	X:1-3,6-11 Y:4,5
X,Y	GB 2143953 A	(SHELL) whole document	X:1-3,6-11 Y:4,5
X,Y	GB 1568968	(RHEEM-) whole document	X:1-3,6-11 Y:4,5
X	FR 2522820 A	(RATION GAZ) see abstract	1-3,6-11
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X	JP 6066948 A	(TOKYO SHIBAURA) see abstract	1-3,6-11
X	JP 62056831 A	(NEW COSMOS) see abstract	1-3,6-11

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
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&	Member of the same patent family		